

REMARKS

Applicants thank the Examiner for confirming in a telephone call on May 8, 2008, that the Office Action mailed December 26, 2007 is a non-final action as indicated on the Office Action Summary page, and not a final office action as indicated on page 5 of the Office Action.

Additionally, Applicants greatly appreciate the telephonic interview of May 21, 2008 with the Examiner and Primary Examiner, in which the obviousness rejection was discussed in detail.

After entry of this amendment, claims 1-30 are pending, of which claims 6-26 and 29-30 are withdrawn. The claims are amended without prejudice to or disclaimer. The amendments to claim 1 find support *inter alia* in the original claims and in the specification, for example, at paragraphs [0019] to [0020] on pages 6-7, paragraphs [0053] to [0069] on pages 11-12, paragraphs [00229]-[00247] on pages 54-59, and Figures 1-13. No new matter has been added.

Withdrawn method claim 11 drawn to the method of using the product depends from the elected product claim or otherwise requires all the limitations of the product claims. Furthermore, linking claim 21 depends from the elected linking product claim or otherwise requires all the limitations of the product claim. In the event the linking product claim is found allowable, then rejoinder of the method claims and the claims dependent from the elected product claim or otherwise requiring all the limitations of the product claims is requested. MPEP § 821.04(b). Additionally, upon allowance of linking claims 1, 11, and 21, withdrawal of the restriction requirement as to the linked inventions is also requested (Groups I-VI, claims 2-10 for linking claim 1; Groups VII-XIV, claims 12-20 and 29-30 for linking claim 11; Groups XV-XIX, claims 22-25 for linking claim 21; see Official Action mailed March 22, 2006). MPEP §§ 809 and 804.01.

Rejections under 35 U.S.C. § 103

Claims 1-4 and 27-28 were rejected under 35 U.S.C. § 103(a) as being obvious over Dujon *et al.* (U.S. Patent 6,395,959; hereinafter "Dujon"). Applicants strongly disagree and respectfully traverse.

The examiner bears the initial burden of establishing *prima facie* obviousness. See *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). To support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. See *In re Lowry*, 32 F.3d 1579, 1582 (Fed. Cir. 1994).

The Examiner alleges that it would be obvious to one of ordinary skill in the art to modify the vector of Dujon by deleting one of the I-SceI sites allegedly resulting in the instant invention. The Examiner further alleges that one would be motivated to do so given that Dujon teaches that either one of the I-SceI sites alone is sufficient to allegedly produce the same transgenic sequence referring to Figure 25B part (1) and (2) of Dujon. Applicants strongly disagree. Figure 25B of Dujon rather teaches that the resulting transgenic sequence from any of the transgenic events *still contains an I-SceI site*, which the Examiner has acknowledged stating that “Dujon et al. do not teach that after recombination the resulting transgenic sequence does not contain any I-SceI site.” (See page 4, first sentence, Office Action mailed December 26, 2007). The claims require that the resulting transgenic sequence does not comprise any recognition site for the enzyme suitable for inducing DNA double-strand breaks. Thus, the teachings of Dujon do not result in the claimed invention. Therefore, because Dujon does not teach or suggest all limitations of the claims as acknowledged by the Examiner, the Examiner has failed to establish *prima facie* obviousness.

Moreover, it is well established that under 35 U.S.C. § 103 the Examiner must consider the reference as a whole, including portions that teach away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). In addition, an Examiner cannot selectively pick and choose from the disclosed parameters without proper motivation as to a particular selection. The mere fact that a reference may be modified to reflect features of the claimed invention does not make the modification, and hence the claimed invention, obvious unless the prior art suggested the desirability of such modification. *In re Mills*, 916 F.2d 680, 682, 16 USPQ2d 1430 (Fed. Cir. 1990); *In re Fritch*, 23 USPQ2d 1780 (Fed. Cir. 1992). Thus, it is impermissible to simply engage in a hindsight reconstruction of the claimed invention where the reference itself provides no teaching as to why the applicant’s combination would have been obvious. *In re Gorman*, 933 F.2d 982, 987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

When considering Dujon as a whole, Dujon teaches that the resulting transgenic sequence from any of the transgenic events *still contains an I-SceI site* as seen in Figure 25B. Furthermore, Dujon at column 7, lines 1-23, explains and confirms that the resulting recombination product is found to the right in Figure 25B, which *contains an I-SceI site*. Dujon has not provided any teaching or suggestion for modifying the resulting transgenic sequence which *contains an I-SceI site* to result in a transgenic sequence that *does not comprise any recognition site* for the enzyme suitable for inducing DNA double-strand breaks as required by the claims. Dujon provides no motivation for modifying the resulting recombination product which *contains an I-SceI site* to one that *does not contain any recognition site*. One skilled in the art reading Dujon would not look to Dujon for teaching a recombinant system that results in a transgenic sequence that *does not comprise any recognition site*, since the resulting product of Dujon all contain an I-SceI site. Thus, because Dujon has not taught such a modification or suggested the desirability of such modification and because the teachings of Dujon do not result in the claimed invention, Dujon does not render the claims obvious without impermissible hindsight.

Furthermore, a recognition sequence which remains in the genome after recombination, as taught by Dujon, would allow for further chromosomal rearrangements or deletions and would render the present recombination system inoperable for its intended purpose. See specification at page 3 paragraph [0009]. Contrary to the teaching of Dujon, the present invention rather describes a system in which the recognition sites are deleted as the result of the homologous recombination event and describes a recombination system that allows for “the repeated, successive application to the same organism.” See page 6 paragraph [0019].

Nevertheless, to expedite prosecution, claim 1 has been amended without prejudice or disclaimer to further characterize the recombination system. In light of the amendments, in the present recombination system of claim 1, the resulting transgenic sequence derived from the transgenic recombination construct does not comprise any recognition site for the enzymes suitable for inducing DNA double-strand breaks. Furthermore, the claims as amended also recite that all recognition sequences for site-directed induction of DNA double-strand breaks are located between homology sequences A and B, in contrast to Dujon which teaches an I-SceI recognition site that is not between the alleged homology sequences, which the Examiner during

the interview stated would likely obviate the rejection. Additionally, the present recombination system allows for the repeated, successive application to the same organism, which the construct of Dujon would be incapable of doing.

For these reasons, reconsideration and withdrawal of the obviousness rejection is respectfully requested for independent claim 1 and the claims dependent therefrom. *See In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988) (holding that if an independent claim is nonobvious then any claim dependent therefrom is nonobvious).


CONCLUSION

For at least the above reasons, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Should the elected product claim be found allowable, Applicants have requested rejoinder of the linked inventions, claims drawn to methods of using the product, and claims which depend from or otherwise include all the limitations of the allowed product claim as explained above.

Accompanying this response is a petition for a two-month extension of time to and including May 27, 2008 pursuant to 37 CFR § 1.7(a) to respond to the Office Action mailed December 26, 2007 with the required fee authorization. No further fee is believed due. If any additional fee is due, please charge our Deposit Account No. 03-2775, under Order No. 13173-00010-US from which the undersigned is authorized to draw.

Respectfully submitted,

By 

Roberte M. D. Makowski, Ph.D.

Registration No.: 55,421

CONNOLLY BOVE LODGE & HUTZ LLP

Correspondence Customer Number: 23416

1007 North Orange Street, P.O. Box 2207

Wilmington, Delaware 19899

(302) 658-9141

(302) 658-5614 (Fax)

Attorney for Applicants